FIG.1

```
      CCGGGTCGACCCACGCGTCCGAAGGCCCCCTCTCACTCCGCTCCACTCCTCGGGCTGG
  5   CTCTCCTGAGGATGCACCAGCGTCACCCCCGGGCAAGATGCCTCCCCTCTGTGTGGC
      CGGAATCCTTGCCTGTGGCTTTCTCCTGGGCTGCTGGGGACCCTCCCATTTCCAGCAGA
      GTTGTCTTCAGGCTTTGGAGCCACAGGCCGTGTCTTCTTACTTGAGCCCTGGTGCTCCC
      TTAAAAGGCCGCCCTCCTTCCCCTGGCTTCCAGAGGCAGAGGCAGAGGCAGAGGCGGG
      CTGCAGGCGGCATCCTACACCTGGAGCTGCTGGTGGCCGTGGGCCCCGATGTCTTCCA
 10   GGCTCACCAGGAGGACACAGAGCGCTATGTGCTCACCAACCTCAACATCGGGGCAGAA
      CTGCTTCGGGACCCGTCCCTGGGGGCTCAGTTTCGGGTGCACCTGGTGAAGATGGTCA
      TTCTGACAGAGCCTGAGGGTGCTCCAAATATCACAGCCAACCTCACCTCGTCCCTGCTG
      AGCGTCTGTGGGTGGAGCCAGACCATCAACCCTGAGGACGACACGGATCCTGGCCATG
      CTGACCTGGTCCTCTATATCACTAGGTTTGACCTGGAGTTGCCTGATGGTAACCGGCAG
 15   GTGCGGGGCGTCACCCAGCTGGGCGGTGCCTGCTCCCCAACCTGGAGCTGCCTCATTA
      CCGAGGACACTGGCTTCGACCTGGGAGTCACCATTGCCCATGAGATTGGGCACAGCTT
      CGGCCTGGAGCACGACGGCGGCCCCGGCAGCGGCTGCGGCCCCAGCGGACACGTGA
      TGGCTTCGGACGGCGCCGCGCCCCGCGCCGGCCTCGCCTGGTCCCCCTGCAGCCGCC
      GGCAGCTGCTGAGCCTGCTCAGCGCAGGACGGGCGCGCTGCGTGTGGGACCCGCCGC
 20   GGCCTCAACCCGGGTCCGCGGGGCACCCGCCGGATGCGCAGCCTGGCCTCTACTACA
      GCGCCAACGAGCAGTGCCGCGTGGCCTTCGGCCCCAAGGCTGTCGCCTGCACCTTCGC
      CAGGGAGCACCTGGATATGTGCCAGGCCCTCTCCTGCCACACAGACCCGCTGGACCAA
      AGCAGCTGCAGCCGCCTCCTCGTTCCTCTCCTGGATGGGACAGAATGTGGCGTGGAGA
      AGTGGTGCTCCAAGGGTCGCTGCCGCTCCCTGGTGGAGCTGACCCCCATAGCAGCAGT
 25   GCATGGGCGCTGGTCTAGCTGGGGTCCCCGAAGTCCTTGCTCCCGCTCCTGCGGAGGA
      GGTGTGGTCACCAGGAGGCGGCAGTGCAACAACCCCAGACCTGCCTTTGGGGGGCGT
      GCATGTGTTGGTGCTGACCTCCAGGCCGAGATGTGCAACACTCAGGCCTGCGAGAAGA
      CCCAGCTGGAGTTCATGTCGCAACAGTGCGCCAGGACCGACGGCCAGCCGCTGCGCTC
      CTCCCCTGGCGGCCGCCTCCTTCTACCACTGGGGTGCTGCTGTACCACACAGCCAAGGG
 30   GATGCTCTGTGCAGACACATGTGCCGGGCCATTGGCGAGAGCTTCATCATGAAGCGTG
      GAGACAGCTTCCTCGATGGGACCCGGTGTATGCCAAGTGGCCCCCGGGAGGACGGGA
      CCCTGAGCCTGTGTGTGTCGGGCAGCTGCAGGACATTGGCTGTGATGGTAGGATGGA
      CTCCCAGCAGGTATGGGACAGGTGCCAGGTGTGTGGTGGGGACAACAGCACGTGCAGC
      CCACGGAAGGGCTCTTTCACAGCTGGCAGAGCGAGAGAATATGTCACGTTTCTGACAGT
 35   TACCCCCAACCTGACCAGTGTCTACATTGCCAACCACAGGCCTCTCTTCACACACTTGG
      CGGTGAGGATCGGAGGGCGCTATGTCGTGGCTGGGAAGATGAGCATCTCCCCTAACAC
      CACCTACCCCTCCCTCCTGGAGGATGGTCGTGTCGAGTACAGAGTGGCCCTCACCGAG
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GACCGGCTGCCCCGCCTGGAGGAGATCCGCATCTGGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTTACAGGCGGTATGGCGAGGAGTATGGCAACCTCACCCGCCCAGACA
TCACCTTCACCTACTTCCAGCCTAAGCCACGGCAGGCCTGGGTGTGGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGGCAGGGCTGCGCTGGGTAAACTACAGCTGCCTG

5 GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCCTGCGTGCTCGAACCCTGCCCTCCCTACTGGGCGGTGGGA
GACTTCGGCCCATGCAGCGCCTCCTGTGGGGGTGGCCTGCGGGAGCGGCCAGTGCGC
TGCGTGGAGGCCCAGGGCAGCCTCCTGAAGACATTGCCCCCAGCCCGGTGCAGAGCA
GGGGCCCAGCAGCCAGCTGTGGCGCTGGAAACCTGCAACCCCCAGCCCTGCCCTGCC

10 AGGTGGGAGGTGTCAGAGCCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGGCAGATGGCCTGGAGGCTCCAGTGACTGAGG
GGCCTGGCTCCGTAGATGAGAAGCTGCCTGCCCCTGAGCCCTGTGTCGGGATGTCATG
TCCTCCAGGCTGGGGCCATCTGGATGCCACCTCTGCAGGGGAGAAGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGGCTCAAGCTGCACACGTGTGGACCCCTGCGGCAGGG

15 TCGTGCTCCGTCTCCTGCGGGCGAGGTCTGATGGAGCTGCGTTTCCTGTGCATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGGCCTGGCAAGCAAGCCTGGGAG
CCGGCGGGAGGTCTGCCAGGCTGTCCCGTGCCCTGCTCGGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGGAGAGGGGTCGTGCGGAGGATCCTGTATTGTGCCCG
GGCCCATGGGGAGGACGATGGTGAGGAGATCCTGTTGGACACCCAGTGCCAGGGGCT

20 GCCTCGCCCGGAACCCCAGGAGGCCTGCAGCCTGGAGCCCTGCCCACCTAGGTGGAA
AGTCATGTCCCTTGGCCCATGTTCGGCCAGCTGTGGCCTTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCGGCCTGT
GCGGCGCTGGTGCGGCCCGAGGCCAGTGTCCCCTGTCTCATTGCCGACTGCACCTACC
GCTGGCATGTTGGCACCTGGATGGAGTGCTCTGTTTCCTGTGGGGATGGCATCCAGCG

25 CCGGCGTGACACCTGCCTCGGACCCCAGGCCCAGGCGCCTGTGCCAGCTGATTTCTGC
CAGCACTTGCCCAAGCCGGTGACTGTGCGTGGCTGCTGGGCTGGGCCCTGTGTGGGAC
AGGGTACGCCCAGCCTGGTGCCCCACGAAGAAGCCGCTGCTCCAGGACGGACCCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCACCTTGAGCCAACAGGAACCATTGACAT
GCGAGGCCCAGGGCAGGCAGACTGTGCAGTGGCCATTGGGCGGCCCCTCGGGGAGGT

30 GGTGACCCTCCGCGTCCTTGAGAGTTCTCTCAACTGCAGTGCGGGGGACATGTTGCTG
CTTTGGGGCCGGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTTCA
GCTCCAAGACCAACACGCTGGTGGTGAGGCAGCGCTGCGGGCGGCCAGGAGGTGGGG
TGCTGCTGCGGTATGGGAGCCAGCTTGCTCCTGAAACCTTCTACAGAGAATGTGACATG
CAGCTCTTTGGGCCCTGGGGTGAAATCGTGAGCCCCTCGCTGAGTCCAGCCACGAGTA

35 ATGCAGGGGGCTGCCGGCTCTTCATTAATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCCATGGGCAGCAGGTGCTCTACTG

GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTCAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCGGGGCCAGTACTGGACCCTCCAATCATGGGTACCGGAGATGCAGGACC
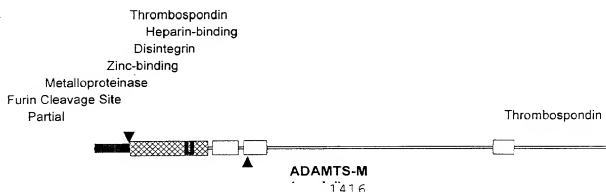CTCAGTCCTGGAAGGGAAAGGAAGGAACC

FIG. 2

PGRPTRPKAPSHSAPLLGLALLRMHQRHPRARCPPLCVAGILACGFLLGCWGPSHFQQSCL
QALEPQAVSSYLSPGAPLKGRPPSPGFQRQRQRQRRAAGGILHLELLVAVGPDVFQAHQED
TERYVLTNLNIGAELLRDPSLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCGWSQTINP
EDDTDPGHADLVLYITRFDLELPDGNRQVRGVTQLGGACSPTWSCLITEDTGFDLGVTIAHEI
GHSFGLEHDGAPGSGCGPSGHVMASDGAAPRAGLAWSPCSRRQLLSLLSAGRARCVWDP
PRPQPGSAGHPPDAQPGLYYSANEQCRVAFGPKAVACTFAREHLDMCQALSCHTDPLDQS
SCSRLLVPLLDGTECGVEKWCSKGRCRSLVELTPIAAVHGRWSSWGPRSPCSRSCGGGVV
TRRRQCNNPRPAFGGRACVGADLQAEMCNTQACEKTQLEFMSQQCARTDGQPLRSSPGG
ASFYHWGAAVPHSQGDALCRHMCRAIGESFIMKRGDSFLDGTRCMPSGPREDGTLSLCVS
GSCRTFGCDGRMDSQQVWDRCQVCGGDNSTCSPRKGSFTAGRAREYVTFLTVTPNLTSV
YIANHRPLFTHLAVRIGGRYVVAGKMSISPNTTYPSLLEDGRVEYRVALTEDRLPRLEEIRIWG
PLQEDADIQVYRRYGEEYGNLTRPDITFTYFQPKPRQAWVWAAVRGPCSVSCGAGLRWVN
YSCLDQARKELVETVQCQGSQQPPAWPEACVLEPCPPYWAVGDFGPCSASCGGGLRERP
VRCVEAQGSLLKTLPPARCRAGAQQPAVALETCNPQPCPARWEVSEPSSCTSAGGAGLAL
ENETCVPGADGLEAPVTEGPGSVDEKLPAPEPCVGMSCPPGWGHLDATSAGEKAPSPWG
SIRTGAQAAHVWTPAAGSCSVSCGRGLMELRFLCMDSALRVPVQEELCGLASKPGSRREV
CQAVPCPARWQYKLAACSVSCGRGVVRRILYCARAHGEDDGEEILLDTQCQGLPRPEPQE
ACSLEPCPPRWKVMSLGPCSASCGLGTARRSVACVQLDQGQDVEVDEAACAALVRPEASV
PCLIADCTYRWHVGTWMECSVSCGDGIQRRRDTCLGPQAQAPVPADFCQHLPKPVTVRGC
WAGPCVGQGTPSLVPHEEAAAPGRTTATPAGACGRQHLEPTGTIDMRGPGQADCAVAIGR
PLGEVVTLRVLESSLNCSAGDMLLLWGRLTWRKMCRKLLDMTFSSKTNTLVVRQRCGRPG
GGVLLRYGSQLAPETFYRECDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAIHAL
ATNMGAGTEGANASYILIRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRG
QYWTLQSWVPEMQDPQSWKGKEGT

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Figure 3

Domain structure of ADAMTS-M and translated nucleic acid sequence. A) Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding motif (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). B) ADAMTS-M nucleotide sequence with translated amino acid sequence above.

A

B

```
  +1  P  G  R  P    T  R  P    K  A  P    S  H  S  A    P  L  L    G  L  A    L  L  R  M    H  Q  R
                                                                      Partial  Prodomain
      ===============================================================================================
  25  CCGGGTCGAC CCACGCGTCC GAAGGCCCCC TCTCACTCCG CTCCACTCCT CGGGCTGGCT CTCCTGAGGA TGCACCAGCG
      GGCCCAGCTG GGTGCGCAGG CTTCCGGGGG AGAGTGAGGC GAGGTGAGGA GCCCGACCGA GAGGACTCCT ACGTGGTCGC

  +1  H  P  R    A  R  C  P    P  L  C    V  A  G    I  L  A  C    G  F  L    L  G  C    W  G  F
                                                                      Partial  Prodomain
      ===============================================================================================
 105  TCACCCCCGG GCAAGATGCC CTCCCCTCTG TGTGGCCGGA ATCCTTGCCT GTGGCTTTCT CCTGGGCTGC TGGGGACCCT
      AGTGGGGGCC CGTTCTACGG GAGGGGAGAC ACACCGGCCT TAGGAACGGA CACCGAAAGA GGACCCGACG ACCCCTGGGA

  +1 S  H  F  Q    Q  S  C    L  Q  A  L    E  P  Q    A  V  S    S  Y  L  S    P  G  A    P  L  K
     Partial  Prodomain
      ===============================================================================================
 185  CCCATTTCCA GCAGAGTTGT CTTCAGGCTT TGGAGCCACA GGCCGTGTCT TCTTACTTGA GCCCTGGTGC TCCCTTAAAA
      GGGTAAAGGT CGTCTCAACA GAAGTCCGAA ACCTCGGTGT CCGGCACAGA AGAATGAACT CGGGACCACG AGGGAATTTT

  +1  G  R  P  P    S  P  G    F  Q  R    Q  R  Q  R    Q  R  R    A  A  G    G  I  L  H    L  E  L
                                          Furin Cleavage  Site  (Motif)
                                                                 ==============
      Partial  Prodomain                                         Metalloproteinase   Domain
      ===============================================================================================
 265  GGCCGCCCTC CTTCCCCTGG CTTCCAGAGG CAGAGGCAGA GGCAGAGGCG GGCTGCAGGC GGCATCCTAC ACCTGGAGCT
      CCGGCGGGAG GAAGGGGACC GAAGGTCTCC GTCTCCGTCT CCGTCTCCGC CCGACGTCCG CCGTAGGATG TGGACCTCGA

  +1  L  V  A    V  G  P  D    V  F  Q    A  H  Q    E  D  T  E    R  Y  V    L  T  N    L  N  I
                                                                      Metalloproteinase   Domain
      ===============================================================================================
 345  GCTGGTGGCC GTGGGCCCCG ATGTCTTCCA GGCTCACCAG GAGGACACAG AGCGCTATGT GCTCACCAAC CTCAACATCG
      CGACCACCGG CACCCGGGGC TACAGAAGGT CCGAGTGGTC CTCCTGTGTC TCGCGATACA CGAGTGGTTG GAGTTGTAGC
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  +1 G   A   E   L   L   R   D   P   S   L   G   A   Q   F   R   V   H   L   V   K   M   V   I   L   T   E   P
                                                                          Metalloproteinase    Domain
     ==========================================================================================================
 425 GGGCAGAACT GCTTCGGGAC CCGTCCCTGG GGGCTCAGTT TCGGGTGCAC CTGGTGAAGA TGGTCATTCT GACAGAGCCT
     CCCGTCTTGA CGAAGCCCTG GGCAGGGACC CCCGAGTCAA AGCCCACGTG GACCACTTCT ACCAGTAAGA CTGTCTCGGA

  +1 E   G   A   P   N   I   T   A   N   L   T   S   S   L   L   S   V   C   G   W   S   Q   T   I   N   P   E
                                                                          Metalloproteinase    Domain
     ----------------------------------------------------------------------------------------------------------
 505 GAGGGTGCTC CAAATATCAC AGCCAACCTC ACCTCGTCCC TGCTGAGCGT CTGTGGGTGG AGCCAGACCA TCAACCCTGA
     CTCCCACGAG GTTTATAGTG TCGGTTGGAG TGGAGCAGGG ACGACTCGCA GACACCCACC TCGGTCTGGT AGTTGGGACT

  +1 D   D   T   D   P   G   H   A   D   L   V   L   Y   I   T   R   F   D   L   E   L   P   D   G   N   R
                                                                Metalloproteinase    Domain
     ==========================================================================================================
 585 GGACGACACG GATCCTGGCC ATGCTGACCT GGTCCTCTAT ATCACTAGGT TTGACCTGGA GTTGCCTGAT GGTAACCGGC
     CCTGCTGTGC CTAGGACCGG TACGACTGGA CCAGGAGATA TAGTGATCCA AACTGGACCT CAACGGACTA CCATTGGCCG

 +10 Q   V   R   G   V   T   Q   L   G   G   A   C   S   P   T   W   S   C   L   I   T   E   D   T   G   F   D
     Metalloproteinase    Domain
     ----------------------------------------------------------------------------------------------------------
 665 AGGTGCGGGG CGTCACCCAG CTGGGCGGTG CCTGCTCCCC AACCTGGAGC TGCCTCATTA CCGAGGACAC TGGCTTCGAC
     TCCACGCCCC GCAGTGGGTC GACCCGCCAC GGACGAGGGG TTGGACCTCG ACGGAGTAAT GGCTCCTGTG ACCGAAGCTG

  +1 L   G   V   T   I   A   H   E   I   G   H   S   F   G   L   E   H   D   G   A   P   G   S   G   C   G   P
                                                                Zinc-binding    Motif
                           =================================================================================
     Metalloproteinase    Domain
     ==========================================================================================================
 745 CTGGGAGTCA CCATTGCCCA TGAGATTGGG CACAGCTTCG GCCTGGAGCA CGACGGCGCG CCCGGCAGCG GCTGCGGCCC
     GACCCTCAGT GGTAACGGGT ACTCTAACCC GTGTCGAAGC CGGACCTCGT GCTGCCGCGC GGGCCGTCGC CGACGCCGGG

  +1 S   G   H   V   M   A   S   D   G   A   A   P   R   A   G   L   A   W   S   P   C   S   R   R   Q   L
     Zinc-binding    Motif
     ==================
     Metalloproteinase    Domain
     ==========================================================================================================
 825 CAGCGGACAC GTGATGGCTT CGGACGGCGG CGCGCCCGC GCCGGCCTCG CCTGGTCCCC CTGCAGCCGC CGGCAGCTGC
     GTCGCCTGTG CACTACCGAA GCCTGCCGCC GCGCGGGCG CGGCCGGAGC GGACCAGGGG GACGTCGGCG GCCGTCGACG

  +1 L   S   L   L   S   A   G   R   A   R   C   V   W   D   P   P   R   P   Q   P   G   S   A   G   H   P   P
     Metalloproteinase    Domain
     ============================================================================
 905 TGAGCCTGCT CAGCGCAGGA CGGGCGCGCT GCGTGTGGGA CCCGCCGCGG CCTCAACCCG GGTCCGCGGG GCACCCGCCG
     ACTCGGACGA GTCGCGTCCT GCCCGCGCGA CGCACACCCT GGGCGGCGCC GGAGTTGGGC CCAGGCGCCC CGTGGGCGGC

  +1 D   A   Q   P   G   L   Y   Y   S   A   N   E   Q   C   R   V   A   F   G   P   K   A   V   A   C   T   F
                                                                                Disintegrin    Domain
                           ================================================================================
 985 GATGCGCAGC CTGGCCTCTA CTACAGCGCC AACGAGCAGT GCCGCGTGGC CTTCGGCCCC AAGGCTGTCG CCTGCACCTT
     CTACGCGTCG GACCGGAGAT GATGTCGCGG TTGCTCGTCA CGGCGCACCG GAAGCCGGGG TTCCGACAGC GGACGTGGAA
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 +1   A   R   E    H   L   D   M    C   Q   A    L   S   C    H   T   D   P    L   D   Q    S   S   C    S   R   L
                              Disintegrin  Domain
           =======================================================================================  ========
1065  CGCCAGGGAG CACCTGGATA TGTGCCAGGC CCTCTCCTGC CACACAGACC CGCTGGACCA AAGCAGCTGC AGCCGCCTCC
      GCGGTCCCTC GTGGACCTAT ACACGGTCCG GGAGAGGACG GTGTGTCTGG GCGACCTGGT TTCGTCGACG TCGGCGGAGG

 +1   L   V   P   L    L   D   G    T   E   C   G    V   E   K    W   C   S    K   G   R   C    R   S   L    V   E   L
      Disintegrin  Domain
      ===================================================================================
1145  TCGTTCCTCT CCTGGATGGG ACAGAATGTG GCGTGGAGAA GTGGTGCTCC AAGGGTCGCT GCCGCTCCCT GGTGGAGCTG
      AGCAAGGAGA GGACCTACCC TGTCTTACAC CGCACCTCTT CACCACGAGG TTCCCAGCGA CGGCGAGGGA CCACCTCGAC

 +1   T   P   I   A    A   V   H    G   R   W    S   S   W   G    P   R   S    P   C   S    R   S   C   G    G   G   V
                                               Heparin-binding  Motif
                                              ====================
                                                          Thrombospondin   Submotif
                            =============================================================================
1225  ACCCCCATAG CAGCAGTGCA TGGGCGCTGG TCTAGCTGGG GAGCCCGAAG TCCTTGCTCC CGCTCCTGCG GAGGAGGTGT
      TGGGGGTATC GTCGTCACGT ACCCGCGACC AGATCGACCC CAGGGGCTTC AGGAACGAGG GCGAGGACGC CTCCTCCACA

 +1   V   T   R    R   R   Q   C    N   N   P    R   P   A    F   G   G   R    A   C   V    G   A   D    L   Q   A
                                   Thrombospondin   Submotif
      =====================================================================================
1305  GGTCACCAGG AGGCGGCAGT GCAACAACCC CAGACCTGCC TTTGGGGGGC GTGCATGTGT TGGTGCTGAC CTCCAGGCCG
      CCAGTGGTCC TCCGCCGTCA CGTTGTTGGG GTCTGGACGG AAACCCCCCG CACGTACACA ACCACGACTG GAGGTCCGGC

 +1   E   M   C   N    T   Q   A    C   E   K   T    Q   L   E    F   M   S    Q   Q   C    A   R   T   D    G   Q   P
      Thrombospondin  Submotif
      ==============================================================================
1385  AGATGTGCAA CACTCAGGCC TGCGAGAAGA CCCAGCTGGA GTTCATGTCG CAACAGTGCG CCAGGACCGA CGGCCAGCCG
      TCTACACGTT GTGAGTCCGG ACGCTCTTCT GGGTCGACCT CAAGTACAGC GTTGTCACGC GGTCCTGGCT GCCGGTCGGC

 +1   L   R   S   S    P   G   G    A   S   F    Y   H   W   G    A   A   V    P   H   S    Q   G   D   A    L   C   R
1465  CTGCGCTCCT CCCCTGGCGG CGCCTCCTTC TACCACTGGG GTGCTGCTGT ACCACACAGC CAAGGGGATG CTCTGTGCAG
      GACGCGAGGA GGGGACCGCC GCGGAGGAAG ATGGTGACCC CACGACGACA TGGTGTGTCG GTTCCCCTAC GAGACACGTC

 +1   H   M   C    R   A   I   G    E   S   F    I   M   K    R   G   D   S    F   L   D    G   T   R    C   M   P
1545  ACACATGTGC CGGGCCATTG GCGAGAGCTT CATCATGAAG CGTGGAGACA GCTTCCTCGA TGGGACCCGG TGTATGCCAA
      TGTGTACACG GCCCGGTAAC CGCTCTCGAA GTAGTACTTC GCACCTCTGT CGAAGGAGCT ACCCTGGGCC ACATACGGTT

 +1   S   G   P   R    E   D   G    T   L   S   L    C   V   S    G   S   C    R   T   F   G    C   D   G    R   M   D
1625  GTGGCCCCCG GGAGGACGGG ACCCTGAGCC TGTGTGTGTC GGGCAGCTGC AGGACATTTG GCTGTGATGG TAGGATGGAC
      CACCGGGGGC CCTCCTGCCC TGGGACTCGG ACACGACACAG CCCGTCGACG TCCTGTAAAC CGACACTACC ATCCTACCTG

 +1   S   Q   Q   V    W   D   R    C   Q   V    C   G   G   D    N   S   T    C   S   P    R   K   G   S    F   T   A
1705  TCCCAGCAGG TATGGGACAG GTGCCAGGTG TGTGGTGGGG ACAACAGCAC GTGCAGCCCA CGGAAGGGCT CTTTCACAGC
      AGGGTCGTCC ATACCCTGTC CACGGTCCAC ACACCACCCC TGTTGTCGTG CACGTCGGGT GCCTTCCCGA GAAAGTGTCG

 +1   G   R   A    R   E   Y   V    T   F   L    T   V   T    P   N   L   T    S   V   Y    I   A   N    H   R   P
1785  TGGCCAGAGCG AGAGAAATATG TCACGTTTCT GACAGTTACC CCCAACCTGA CCAGTGTCTA CATTGCCAAC CACAGGCCTC
      ACCGGTCTCGC TCTCTTATAC AGTGCAAAGA CTGTCAATGA GGGTTGGACT GGTCACAGAT GTAACGGTTG GTGTCCGGAG
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    +1 L  F  T  H   L  A  V  R   I  G  G  R   Y  V  A  G   K  M  S  I   S  P  N   T  T  Y
1865 TCTTCACACA CTTGGCGGTG AGGATCGGAG GGCGCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCCTAA CACCACCTAC
     AGAAGTGTGT GAACCGCCAC TCCTAGCCTC CCGCGATACA GCACCGACCC TTCTACTCGT AGAGGGGATT GTGGTGGATG


    +1 P  S  L  L   E  D  G  R   V  E  Y  R   V  A  L  T   E  D  R  L   P  R  L  E   E  I  R
1945 CCCTCCCTCC TGGAGGATGG TCGTGTCGAG TACAGAGTGG CCCTCACCGA GGACCGGCTG CCCCGCCTGG AGGAGATCCG
     GGGAGGGAGG ACCTCCTACC AGCACAGCTC ATGTCTCACC GGGAGTGGCT CCTGGCCGAC GGGGCGGACC TCCTCTAGGC


    +1 I  W  G  P   L  Q  E  D   A  D  I  Q   V  Y  R  R   Y  G  E  E   Y  G  N   L  T  R
2025 CATCTGGGGA CCCCTCCAGG AAGATGCTGA CATCCAGGTT TACAGGCGGT ATGGCGAGGA GTATGGCAAC CTCACCCGCC
     GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCA TACCGCTCCT CATACCGTTG GAGTGGGCGG


    +1 P  D  I  T   F  T  Y  F   Q  P  K  P   R  Q  A  W   V  W  A  A   V  R  G  P   C  S  V
2105 CAGACATCAC CTTCACCTAC TTCCAGCCTA AGCCACGGCA GGCCTGGGTG TGGGCCGCTG TGCGTGGGCC CTGCTCGGTG
     GTCTGTAGTG GAAGTGGATG AAGGTCGGAT TCGGTGCCGT CCGGACCCAC ACCCGGCGAC ACGCACCCGG GACGAGCCAC


    +1 S  C  G  A   G  L  R  W   V  N  Y  S   C  L  D  Q   A  R  K  E   L  V  E  T   V  Q  C
2185 AGCTGTGGGG CAGGGCTGCG CTGGGTAAAC TACAGCTGCC TGGACCAGGC CAGGAAGGAG TTGGTGGAGA CTGTCCAGTG
     TCGACACCCC GTCCCGACGC GACCCATTTG ATGTCGACGG ACCTGGTCCG GTCCTTCCTC AACCACCTCT GACAGGTCAC


    +1 Q  G  S  Q   Q  P  P  A   W  P  E  A   C  V  L  E   P  C  P  P   Y  W  A   V  G  D
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCCTGC GTGCTCGAAC CCTGCCCTCC CTACTGGGCG GTGGGAGACT
     GGTTCCCTCG GTCGTCGGTG GTCGCACCGG TCTCCGGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCCTCTGA


    +1 F  G  P  C   S  A  S  C   G  G  G  L   R  E  R  P   V  R  C  V   E  A  Q  G   S  L  L
2345 TCGGCCCATG CAGCGCCTCC TGTGGGGGTG GCCTGCGGGA GCGGCCAGTG CGCTGCGTGG AGGCCCAGGG CAGCCTCCTG
     AGCCGGGTAC GTCGCGGAGG ACACCCCCAC CGGACGCCCT CGCCGGTCAC GCGACGCACC TCCGGGTCCC GTCGGAGGAC


    +1 K  T  L  P   P  A  R  C   R  A  G  A   Q  Q  F  A   V  A  L  E   T  C  N  F   Q  P  C
2425 AAGACATTGC CCCCAGCCCG GTGCAGAGCA GGGGCCCAGC AGCCAGCTGT GGCGCTGGAA ACCTGCAACC CCCAGCCCTG
     TTCTGTAACG GGGGTCGGGC CACGTCTCGT CCCCGGGTCG TCGGTCGACA CCGCGACCTT TGGACGTTGG GGGTCGGGAC


    +1 P  A  R  W   E  V  S  E   P  S  S  C   T  S  A  G   G  A  G  L   A  L  E   N  E  T
2505 CCCTGCCAGG TGGGAGGTGT CAGAGCCCAG TCATGCACGA TCAGCTGGTG GAGCAGGCCT GGCCTTGGAG AACGAGACCT
     GGGACGGTCC ACCCTCCACA GTCTCGGGTC AGTACGTGCT AGTCGACCAC CTCGTCCGGA CCGGAACCTC TTGCTCTGGA


    +1 C  V  P  G   A  D  G  L   E  A  P  V   T  E  G  P   G  S  V  D   E  K  L  P   A  P  E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTGACTGA GGGGCCTGGC TCCGTAGATG AGAAGCTGCC TGCCCCTGAG
     CACACGGTCC CCGTCTACCG GACCTCCGAG GTCACTGACT CCCCGGACCG AGGCATCTAC TCTTCGACGG ACGGGGACTC


    +1 P  C  V  G   M  S  C  P   P  G  W  G   H  L  D  A   T  S  A  G   E  K  A  P   S  P  W
2665 CCCTGTGTCG GGATGTCATG TCCTCCAGGC TGGGGCCATC TGGATGCCAC CTCTGCAGGG GAGAAGGCTC CCTCCCCATG
     GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCCGGTAG ACCTACGGTG GAGACGTCCC CTCTTCCGAG GGAGGGGTAC


    +1 G  S  I  R   T  G  A  Q   A  A  H  V   W  T  P  A   A  G  S  C   S  V  S   C  G  R
2745 GGGCAGCATC AGGACGGGGC CTCAAGCTGC ACACGTGTGG ACCCCTGCGG CAGGGTCGTG TCCGTCTCCT GCGGGGCGAG
     CCCGTCGTAG TCCTGCCCCG GAGTTCGACG TGTGCACACC TGGGGACGCC GTCCCAGCAC AGGCAGAGG ACGCCCGCTC


    +1 G  L  M  E   L  R  F  L   C  M  D  S   A  L  R  V   P  V  Q  E   E  L  C  G   L  A  S
2825 GTCTGATGGA GCTGCGTTTC CTGTGCATGG ACTCTGCCCT CAGGGTGCCT GTCCAGGAAG AGCTGTGTGG CCTGGCAAGC
     CAGACTACCT CGACGCAAAG GACACGTACC TGAGACGGGA GTCCCACGGA CAGGTCCTTC TCGACACACC GGACCGTTCG
```

```
  +1   K   P   G   S   R   R   E   V   C   Q   A   V   P   C   P   A   R   W   Q   Y   K   L   A   A   C   S
2905 AAGCCTGGGA GCCGGCGGGA GGTCTGCCAG GCTGTCCCGT GCCCTGCTCG GTGGCAGTAC AAGCTGGCGG CCTGCAGCGT
     TTCGGACCCT CGGCCGCCCT CCAGACGGTC CGACACGGGCA CGGGACGAGC CACCGTCATG TTCGACCGCC GGACGTCGCA
```

```
  +1   S   C   G   R   G   V   V   R   R   I   L   Y   C   A   R   A   H   G   E   D   D   G   E   E   I   L
2985 GAGCTGTGGG AGAGGGGTCG TGCGGAGGAT CCTGTATTGT GCCCGGGCCC ATGGGGAGGA CGATGGTGAG GAGATCCTGT
     CTCGACACCC TCTCCCCAGC ACGCCTCCTA GGACATAACA CGGGCCCGGG TACCCCTCCT GCTACCACTC CTCTAGGACA
```

```
  +1   L   D   T   Q   C   Q   G   L   P   R   P   E   P   Q   E   A   C   S   L   E   P   C   P   P   R   W   K
3065 TGGACACCCA GTGCCAGGGG CTGCCTCGCC CGGAACCCCA GGAGGCCTGC AGCCTGGAGC CCTGCCCACC TAGGTGGAAA
     ACCTGTGGGT CACGGTCCCC GACGGAGCGG GCCTTGGGGT CCTCCGGACG TCGGACCTCG GGACGGGTGG ATCCACCTTT
```

```
  +1   V   M   S   L   G   P   C   S   A   S   C   G   L   G   T   A   R   R   S   V   A   C   V   Q   L   D   Q
3145 GTCATGTCCC TTGGCCCATG TTCGGCCAGC TGTGGCCTTG GCACTGCTAG ACGCTCGGTG GCCTGTGTGC AGCTCGACCA
     CAGTACAGGG AACCGGGTAC AAGCCGGTCG ACACCGGAAC CGTGACGATC TGCGAGCCAC CGGACACACG TCGAGCTGGT
```

```
  +1   G   Q   D   V   E   V   D   E   A   A   C   A   A   L   V   R   P   E   A   S   V   P   C   L   I   A
3225 AGGCCAGGAC GTGGAGGTGG ACGAGGCGGC CTGTGCGGCG CTGGTGCGAC CGGAGGCCAG TGTCCCCTGT CTCATTGCCG
     TCCGGTCCTG CACCTCCACC TGCTCCGCCG GACACGCCGC GACCACGCCG GGCTCCGGTC ACAGGGGACA GAGTAACGGC
```

```
  +1 D   C   T   Y   R   W   H   V   G   T   W   M   E   C   S   V   S   C   G   D   G   I   Q   R   R   R   D
                                                                 Thrombospondin    Submotif
                     ==================================================================================
3305 ACTGCACCTA CCGCTGGCAT GTTGGCACCT GGATGGAGTG CTCTGTTTCC TGTGGGGATG GCATCCAGCG CCGGCGTGAC
     TGACGTGGAT GGCGACCGTA CAACCGTGGA CCTACCTCAC GAGACAAAGG ACACCCCTAC CGTAGGTCGC GGCCGCACTG
```

```
  +1   T   C   L   G   P   Q   A   Q   A   P   V   P   A   D   F   C   Q   H   L   P   K   P   V   T   V   R   G
                    Thrombospondin    Submotif
     =================================================================================================
3385 ACCTGCCTCG GACCCCAGGC CCAGGCGCCT GTGCCAGCTG ATTTCTGCCA GCACTTGCCC AAGCCGGTGA CTGTGCGTGG
     TGGACGGAGC CTGGGGTCCG GGTCCGCGGA CACGGTCGAC TAAAGACGGT CGTGAACGGG TTCGGCCACT GACACGCACC
```

```
  +1   C   W   A   G   P   C   V   G   Q   G   T   P   S   L   V   P   H   E   E   A   A   A   P   G   R   T
       Thrombospondin    Submotif
       ===============================
3465 CTGCTGGGCT GGGCCCTGTG TGGGACAGGG TACGCCCAGC CTGGTGCCCC ACGAAGAAGC CGCTGCTCCA GGACGGACCA
     GACGACCCGA CCCGGGACAC ACCCTGTCCC ATGCGGGTCG GACCACGGGG TGCTTCTTCG GCGACGAGGT CCTGCCTGGT
```

```
  +1 T   A   T   P   A   G   A   C   G   R   Q   H   L   E   P   T   G   T   I   D   M   R   G   P   G   Q   A
3545 CAGCCACCCC TGCTGGTGCC TGTGGCAGGC AGCACCTTGA GCCAACAGGA ACCATTGACA TGCGAGGCCC AGGGCAGGCA
     GTCGGTGGGG ACGACCACGG ACACCGTCCG TCGTGGAACT CGGTTGTCCT TGGTAACTGT ACGCTCCGGG TCCCGTCCGT
```

```
  +1   D   C   A   V   A   I   G   R   P   L   G   E   V   V   T   L   R   V   L   E   S   S   L   N   C   S   A
3625 GACTGTGCAG TGGCCATTGG GCGGCCCCTC GGGGAGGTGG TGACCCTCCG CGTCCTTGAG AGTTCTCTCA ACTGCAGTGC
     CTGACACGTC ACCGGTAACC CGCCGGGGAG CCCCTCCACC ACTGGGAGGC GCAGGAACTC TCAAGAGAGT TGACGTCACG
```

```
  +1   G   D   M   L   L   L   W   G   R   L   T   W   R   K   M   C   R   K   L   L   D   M   T   F   S   S
3705 GGGGGACATG TTGCTGCTTT GGGGCCGGCT CACCTGGAGG AAGATGTGCA GGAAGCTGTT GGACATGACT TTCAGCTCCA
     CCCCCTGTAC AACGACGAAA CCCCGGCCGA GTGGACCTCC TTCTACACGT CCTTCGACAA CCTGTACTGA AAGTCGAGGT
```

```
  +1 K   T   N   T   L   V   V   R   Q   R   C   G   R   P   G   G   G   V   L   L   R   Y   G   S   Q   L   A
3785 AGACCAACAC GCTGGTGGTG AGGCAGCGCT GCGGGCGGCC AGGAGGTGGG GTGCTGCTGC GGTATGGGAG CCAGCTTGCT
     TCTGGTTGTG CGACCACCAC TCCGTCGCGA CGCCCGCCGG TCCTCCACCC CACGACGACG CCATACCCTC GGTCGAACGA
```

```
 +1  P   E   T   F   Y   R   E   C   D   M   Q   L   F   G   P   W   G   E   I   V   S   P   S   L   S   P   A
3865 CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTTG GGCCCTGGGG TGAAATCGTG AGCCCCTCGC TGAGTCCAGC
     GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAAC CCGGGACCCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTCG

 +1  T   S   N   A   G   G   C   R   L   F   I   N   V   A   P   H   A   R   I   A   I   H   A   L   A   T
3945 CACGAGTAAT GCAGGGGGCT GCCGGCTCTT CATTAATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
     GTGCTCATTA CGTCCCCCGA CGGCCGAGAA GTAATTACAC CGAGGCGTGC GTGCCTAACG GTAGGTACGG GACCGGTGGT

 +1 N   M   G   A   G   T   E   G   A   N   A   S   Y   I   L   I   R   D   T   H   S   L   R   T   T   A   F
4025 ACATGGGCGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCGGG GACACCCACA GCTTGAGGAC CACAGCGTTC
     TGTACCCGCG ACCCTGGCTC CCTCGGTTAC GGTCGATGTA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTCGCAAG

 +1  H   G   Q   Q   V   L   Y   W   E   S   E   S   S   Q   A   E   M   E   F   S   E   G   F   L   K   A   Q
4105 CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTTCAGC GAGGGCTTCC TGAAGGCTCA
     GTACCCGTCG TCCACGAGAT GACCCTCAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT

 +1  A   S   L   R   G   Q   Y   W   T   L   Q   S   W   V   P   E   M   Q   D   P   Q   S   W   K   G   K
4185 GGCCAGCCTG CGGGGCCAGT ACTGGACCCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCCTGG AAGGGAAAGG
     CCGGTCGGAC GCCCCGGTCA TGACCTGGGA GGTTAGTACC CATGGCCTCT ACGTCCTGGG AGTCAGGACC TTCCCTTTCC

 +1 E   G   T
4265 AAGGAACC
     TTCCTTGG
```

Fig. 4

Metalloproteinase Domain Alignment of ADAMTS-M v. ADAMTS Family

Percent Homology
Sim   Ident

360

hADAMTS-4(AB014588)	(202)	
hADAMTS-5(AF142099)	(241)	
hADAMTS-1(AF060152)	(220)	
hADAMTS-8(AF060153)	(199)	
hADAMTS-2(AJ003125)	(248)	
M1-MPD	(1)	
Consensus	(301)	

Sim / Ident: 38, 44, 28, 46, 32

420

hADAMTS-4(AB014588)	(251)
hADAMTS-5(AF142099)	(299)
hADAMTS-1(AF060152)	(274)
hADAMTS-8(AF060153)	(253)
hADAMTS-2(AJ003125)	(300)
M1-MPD	(39)
Consensus	(361)

49   32

480

hADAMTS-4(AB014588)	(310)
hADAMTS-5(AF142099)	(358)
hADAMTS-1(AF060152)	(333)
hADAMTS-8(AF060153)	(312)
hADAMTS-2(AJ003125)	(360)
M1-MPD	(98)
Consensus	(421)

63   48   (TS-4 v. TS-5)

540

hADAMTS-4(AB014588)	(369)
hADAMTS-5(AF142099)	(417)
hADAMTS-1(AF060152)	(392)
hADAMTS-8(AF060153)	(372)
hADAMTS-2(AJ003125)	(416)
M1-MPD	(159)
Consensus	(481)

```
                                        541                                                          600
hADAMTS-4(AB014588)   (429) E.P--LHDIVTF...-KDV....DR.QL.KG.SH....--QLPPP.A.M.SGHLN.HAM.
hADAMTS-5(AF142099)   (476) RKQ--ILG.E....-QP...YC..NL..EYSVQ...--GMDV.E..K.AVVR.Q.MV.
hADAMTS-1(AF060152)   (451) QNP--IC..GD...-TS.C.NR.Q.FF.E.SRK.P--DAA.T.ST..TGTSGG.VLV.
hADAMTS-8(AF060153)   (431) G.A--LP.T.G.E.NAL.Q.DQ..ROF..R..N.NTSA.QV.DQ.C.CN-T.GABPI.
hADAMTS-2(AJ003125)   (471) FRLDWPALN-QH.A--LH..MDE..RFD..G.YMO..AFRTF...Q..QG.S--HP.N.YF.
M1-MPD                (213) R.-------------
Consensus             (541)  A      LP  LKg    YDA   QC   TFGPD  HCP    D  CA  LWC     G    C
```